

Economic Consequences of Renal Dysfunction among Cardiopulmonary Bypass Surgery Patients: A Hospital-Based Perspective

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ABSTRACT

Background: Renal dysfunction is common after cardiopulmonary bypass procedures and is associated with higher mortality rates and longer lengths of stay. However, less is known about the actual cost of care for these patients. We sought to quantify the hospital costs attributed to renal dysfunction in cardiopulmonary bypass patients at a large academic referral center.

Methods: All patients undergoing cardiopulmonary bypass procedures were identified through administrative databases for a 3-year study period. Renal failure was defined using laboratory values from the hospitalization. Total direct costs and costs by hospital department were determined using the hospital cost-accounting system. A multivariate linear model was developed to determine total direct hospital costs after cardiopulmonary bypass procedures after adjusting for relevant clinical and demographic variables.

Results: Nine percent of the study population developed

new-onset renal dysfunction, and 18% of patients overall undergoing cardiopulmonary bypass experienced renal dysfunction during the hospitalization. Direct costs were 42% higher for patients with renal dysfunction, an average of \$5807 per case. Higher costs were noted in intensive care unit use and pharmacy, laboratory, and radiology services.

Conclusions: Renal dysfunction increases the direct hospital costs of care, even after adjustment for age, sex, race, and comorbidities. Nationwide, we estimate that renal dysfunction may add up to \$643 million in hospital costs for caring for cardiopulmonary bypass patients. Interventions designed to reduce the incidence and severity of renal dysfunction may significantly reduce hospital costs for these patients.

Keywords: cardiopulmonary bypass surgery, economic evaluation, outcomes research, renal dysfunction.

Introduction

Cardiopulmonary bypass surgical procedures are common and expensive and may have significant complications associated with the procedure. For example, coronary artery bypass grafting (CABG) annually accounts for an estimated 607,000 operations, with an average total cost per case of \$44,820 [1]. Over the past 20 years, the volume of CABG procedures has grown markedly, with the most significant growth occurring among older patient pop-

ulations [2–7]. Between 1987 and 1996, for example, CABG rates in the United States rose by 18% among patients aged 65 years or older and by 67% among those aged 80 years or older [8,9]. Coincident with this older demographic is a patient population that has a higher burden of cardiac and noncardiac comorbid illness [10] as well as higher rates of postsurgical complications.

Major complications after cardiopulmonary bypass include myocardial infarction, stroke, and renal failure and are generally the result of insufficient end-organ perfusion during cardiopulmonary bypass [11–13]. Hammermeister et al. [14] evaluated over 10,000 patients undergoing CABG at Veterans Administration medical centers between 1987 and 1989. In this study, investigators found that 15% of patients had one or more ischemia-related complications. In terms of renal impairment

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specifically, several studies have shown that patients who have undergone cardiac surgery develop decreased renal blood flow and significantly reduced glomerular filtration rates [15–17]. The impact of these phenomena on clinical and cost outcomes are not well understood but are thought to be considerable.

Acute renal failure is a frequent complication of operations utilizing cardiopulmonary bypass [18–21]. Moderate reversible renal dysfunction occurs after 30% of these procedures and is associated with mortality rates ranging from 7% to 38% [16,20–23]. However, approximately 5% of post-cardiopulmonary bypass patients will develop severe postsurgical renal failure requiring hemodialysis. In this latter subgroup, all-cause mortality is considerably higher and ranges from 50% to 90% [10,16,20–22]. Mortality among these patients requiring acute hemodialysis is attributable not only to a loss of renal function but also to high rates of secondary complications, such as central nervous system dysfunction, sepsis, and gastrointestinal bleeding [23,24].

Despite the impact that renal dysfunction has on clinical outcomes and length of stay [13], relatively little is known about the economic consequence of renal dysfunction after cardiopulmonary bypass surgery. Prior studies analyzing the costs associated with CABG surgery have generally identified two populations of patients—“low-cost” (\$16,000–\$20,000) and “high-cost” (\$40,000–\$80,000) subgroups [25]. Costs in the high-cost subgroup, not surprisingly, have been shown to be driven by severe and usually multiple postoperative complications. However, the specific role of renal dysfunction on hospital costs is unknown.

The purpose of this study was threefold: 1) to estimate the impact of renal dysfunction on total direct hospital costs in cardiopulmonary bypass patients; 2) to stratify that analysis by the type of renal dysfunction, and 3) to identify which hospital cost centers were the primary drivers of increased costs associated with renal dysfunction.

Methods

Setting, Patient Selection, and Data Sources

The setting for this study was New York Presbyterian Hospital–Weill Cornell Campus, a tertiary care academic medical center in New York City. Using administrative data, we identified all patients (N = 3493) undergoing cardiopulmonary bypass procedures based on DRG assignment (DRGs 104–107 and 109) for the study years 1998 to 2000. Patients

under the age of 18 and with missing cost data were excluded.

Serum creatinine values were collected on the entire population (N = 3493) and used to classify cases into one of four renal function categories as described later. We then selected a random sample of 1000 cases, representing 28% of myocardial revascularization procedures performed during the study period. Thirty-one cases were excluded based on the above criteria, leaving a total study sample of 969 cases. No statistically significant clinical or demographic differences were observed between our study sample (N = 969) and our base population (N = 3493) (data not shown). To have sufficient samples in each of the four study subgroups (see definitions of renal dysfunction later), we over-sampled for patients with renal dysfunction.

Serum creatinine values, used to classify cases into one of four renal function categories, were obtained from the clinical information system. Demographic data, ICD-9 codes, total direct hospital costs, and direct costs by hospital cost center were electronically obtained from an institutional administrative and cost accounting data set (The Transition Systems, Inc. [TSI], Iowa City, IA).

An IRB exemption was obtained for this study, because the data collection was limited to anonymous retrospective administrative data review.

Definitions of Renal Dysfunction and Comorbidity Classifications

Serum creatinine values were obtained by manual review of laboratory data for each case included in our sample. Hospital admission dates for myocardial revascularization procedures were matched to corresponding laboratory data. For each hospitalization, three serum creatinine values were recorded: 1) admission serum creatinine; 2) highest serum creatinine during the hospitalization, and 3) discharge serum creatinine. Cases were then classified into one of four categories based on the following criteria: 1) normal renal function—all three serum creatinine measurements ≤ 1.5 mg/dl; 2) presurgical renal dysfunction (stable)—admission creatinine > 1.5 mg/dl and other two measurements did not exceed 25% of baseline admission creatinine; and 3) presurgical renal dysfunction (worsening)—admission creatinine > 1.5 mg/dl and at least one of the other two creatinine measurements exceeded baseline admission creatinine by 25%; and 4) postsurgical renal dysfunction—admission creatinine measurement ≤ 1.5 mg/dl and at least one of the other two creatinine measurements > 1.5 mg/dl. Comorbidity illness classification was

determined using ICD-9 description codes and the comorbidity scale of Charlson et al. [26] as modified by Deyo et al. [27].

Cost Identification Methods

All costs are presented in FY2000 USD using the M-CPI and obtained after patient discharge. Cost data were electronically acquired from TSI, the institutional cost-accounting system. In TSI, costs are derived from individual patient charges with the application of department-specific cost-to-charge ratios used for Medicare reporting [28,29]. Total direct costs were defined according to the TSI format and included all patient service, nursing, and technical personnel costs as well as supplies.

TSI includes several hundred cost centers; these cost centers were consolidated into 18 department-level cost centers to analyze the main drivers of costs in patients with renal dysfunction. Additionally, for this analysis, direct medical costs included costs for the use of inpatient wards, operating rooms, intensive care units (ICUs), pharmaceuticals, laboratory services, and radiologic services. All professional fees were excluded.

Statistical Methods

We used descriptive statistics (SAS System v6.12, SAS Institute Inc., Cary, NC) to characterize our study population. For this analysis, our dependent outcome of interest was total direct hospital costs (log TDHC). Univariate measures of association were then tested between our primary outcome variable, log TDHC, and each of the demographic and clinical independent variables. The demographic variables included age, sex, and race (white vs. nonwhite). Clinical variables included renal function classification and comorbidity score (see above: "Definitions of Renal Dysfunction and Comorbidity Classifications").

Univariate measures of association for categorical variables were calculated using Fisher's exact test. Univariate measures of association for continuous variables were tested using either Student's *t* test (parametric) or Wilcoxon's rank sum (non-parametric) test. A multivariable linear model was then developed to generate the adjusted geometric means for log TDHC, our dependent variable. To improve the efficiency of the statistical model, we employed a log transformation to TDHC to follow the implicit statistical assumptions of normality. Using a general linear model (Proc GLM), we selected the best model by applying a stepwise regression with a threshold of $P \leq .01$ for selection and stay. The final multivariable model included

age, sex, race, comorbidity score, and renal dysfunction category. There were no statistically significant interaction terms identified in the model.

Collinearity diagnostics were performed with a detailed analysis of collinearity among the regressors including eigenvalues, condition indexes, and decomposition of the variances of the estimates with respect to each eigenvalue, and there was no resulting evidence of multicollinearity. No explanatory variable was found to be a near-linear combination of other explanatory variables in the model. Specifically, no component of the model was associated with a condition index greater than 18 (whereas a condition index of 30–100 indicates moderate-to-strong collinearity).

We also tested the model for heteroskedasticity (i.e., increasing or decreasing variation in the residuals with fitted values) using fitted values of log TDHC by first examining a plot of the residuals versus the fitted values. No unusual pattern was discerned from this plot. As well, we performed the Cook-Weisberg test for heteroskedasticity using fitted values of log TDHC, and there was no evidence to suggest a departure from the null hypothesis of constant variance ($P > .05$).

Least-squares means and their respective confidence intervals (CIs) are presented as back-transformed (exponentiated) values (i.e., geometric means). We also report pairwise comparisons of the adjusted geometric means for log TDHC between each of the four renal function subgroups. All presented *P* values are two-tailed with statistical significance evaluated at the 0.05 alpha level.

Results

A schematic of our study sample is shown in Fig. 1. From the original 3-year study population ($N = 3493$), 633 patients (18%) undergoing cardiopulmonary bypass experienced renal dysfunction during the surgical hospitalization period. Approximately half of these patients ($N = 311$; 49%) developed new-onset renal dysfunction. From this population, we then selected a random sample of cases, oversampling for patients with renal dysfunction to have a sufficient sample in each of the four study subgroups for our cost analysis.

Table 1 shows the demographic and clinical characteristics of the study population. The overall rate of renal dysfunction in the cardiopulmonary bypass population at our study institution was 18% after adjusting for the oversampling of patients with renal dysfunction. Patients were stratified into four groups as previously defined: 1) normal renal

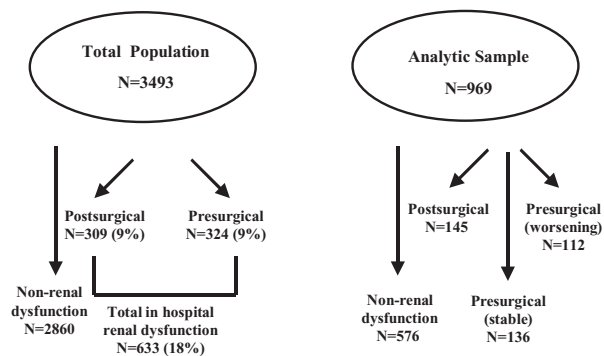


Figure 1 Schematic of total population and analytic sample. Total population represents all adult patients (N = 3493) undergoing cardiopulmonary bypass procedures based on DRG assignment (DRGs 104–107 and 109) for the study years 1998–2000. Analytic sample represents a random sample of 1000 cases (28% of total population), oversampled for patients with renal dysfunction. Subgroup classifications and definitions of renal dysfunction are given in the text.

function, 2) presurgical renal dysfunction (stable); 3) presurgical renal dysfunction (worsening); and 4) postsurgical renal dysfunction. From these data, patients with renal dysfunction were more likely to be female, older, and members of minority groups. Furthermore, the comorbidity scores were higher in patients with renal dysfunction than in patients without renal impairment. Renal dysfunction was also associated with longer unadjusted lengths of stay and higher in-hospital mortality rates for all three subgroups when compared to patients with normal renal function.

We next examined which demographic and clinical

characteristics were associated with increased total direct hospital costs. Age, sex (being female), higher comorbidity score, nonwhite race, and renal dysfunction were all significantly associated with higher costs (data not shown). A multivariate linear model of log TDHC was developed as described above. In this model, age, sex, race, renal dysfunction, and comorbidity score remained and were used to produce adjusted total direct costs. The parameters of this model are shown in Table 2. Renal dysfunction demonstrated the strongest univariate association with total direct costs ($P < .001$) and was used to guide our stratified analysis.

We stratified our cost analysis by renal function classification and report risk-adjusted geometric means and 95% CI as described above. As shown in Fig. 2, in patients with normal renal function, the TDHC averaged \$13,708 (mean \$12,944; 95% CI \$14,519) after cardiopulmonary bypass procedures. For patients with new-onset, postsurgical renal dysfunction, the THDC averaged \$18,834 (mean \$17,049; 95% CI \$20,805), increasing costs by 34% when compared to normal patients. Patients with pre-existing renal dysfunction demonstrated worse economic outcomes. Patients with presurgical but stable renal dysfunction averaged \$19,539 (mean \$17,713; 95% CI \$21,553) in adjusted TDHC, while patients with presurgical but worsening renal dysfunction averaged \$22,110 (mean \$19,848; 95% CI \$24,631). Further, all renal dysfunction models demonstrated statistically significant differences in adjusted log TDHC when

Table 1 Clinical and demographic characteristics of study population

	Total*	Normal renal function*	Postsurgical RD*	Presurgical RD	
				Stable*	Worsening*
N (% of total)†*	969 (100)	576 (59.4)	145 (15)	136 (14)	112 (11.6)
Age (years)	67.89 ± 11.70	66.36 ± 11.62	72.05 ± 10.58‡	67.96 ± 11.89	70.30 ± 11.74‡
% Female	32.30	37.15	22.07‡	30.15	23.21§
Comorbidity score	1.01 ± 1.07	0.81 ± 0.94	1.19 ± 1.08‡	1.42 ± 1.34‡	1.28 ± 1.13‡
Admit creatinine	1.69 ± 1.85	0.90 ± 0.25	1.18 ± 0.24‡	4.35 ± 3.09‡	3.17 ± 1.80‡
Peak creatinine	2.17 ± 2.27	1.05 ± 0.23	2.15 ± 0.79‡	4.58 ± 3.31‡	5.07 ± 2.0‡
% Minority	33.95	33.50	26.21	36.03	43.75
Length of stay (days)	11.76 ± 7.12	9.71 ± 4.97	14.48 ± 8.55‡	13.21 ± 7.17‡	17.05 ± 9.74‡
Mortality (%)	3.41	0.70	5.52‡	6.62‡	10.71‡
Mean direct cost (unadjusted)	18,238 ± 13,405	14,972 ± 11,015	21,733 ± 14,246‡	22,864 ± 15,504‡	24,890 ± 15,515‡

Note: Clinical and demographic characteristics of four study subgroups: 1) normal renal function; 2) postsurgical renal dysfunction; 3) presurgical renal dysfunction (stable); and 4) presurgical renal dysfunction (worsening). Definitions for the four subgroups can be found in the text. Statistical significance reflects pairwise comparisons to the normal renal function subgroup. Statistical comparisons were made using the following analyses: 1) Student's *t* test (age, comorbidity score, admit creatinine, peak creatinine, and mean direct cost); 2) chi-square (% female and % minority); and 3) Wilcoxon rank-sum (length of stay).

*Mean ± SD.

†Study population is oversampled for renal dysfunction.

‡ $P \leq .0001$.

§ $P < .001$.

Abbreviation: RD, renal dysfunction.

Table 2 Multivariate model of total direct hospital costs

Independent variable	Beta coefficient	Standard error	P value
Age*	0.0065	0.0016	<.0001
Sex†	0.1768	0.0397	<.0001
Race‡	0.0616	0.0395	.12
Comorbidity score			
1§	0.0875	0.0427	.04
2§	0.1784	0.0545	.001
≥3§	0.1866	0.0716	.009
Postsurgical renal disease	0.3213	0.0541	<.0001
Presurgical renal disease			
Stable	0.3550	0.0551	<.0001
Worsening	0.4787	0.0599	<.0001

Note: A multivariable linear model was then developed to generate the adjusted geometric means for log TDHC, our dependent variable. Covariates included in the final model included age, sex, race, and comorbidity score (classification of Deyo et al. [27]) and renal dysfunction category. Model parameters and P values are shown.

*Treated as a continuous variable in model.

†Male (referent) vs. female.

‡White (referent) vs. nonwhite.

§Referent group: comorbidity score = 0.

||Referent group: normal renal function.

compared to the normal renal function model ($P < .001$).

We next examined the sources of increased costs for all patients with renal dysfunction compared to patients with normal renal function. In this analysis, we identified several important drivers of the increased cost associated with renal dysfunction, including ICU costs (\$6764 vs. \$3988), pharmacy (\$2191 vs. \$952), laboratory testing (\$1167 vs.

\$728), and radiology services (\$441 vs. \$247) ($P < .05$ for all comparisons). Operating room costs were not significantly different between the two groups (\$5587 vs. \$5010). The 13 other department-level cost centers were similar between subgroups.

Renal dysfunction patients in all three subgroups also incurred significantly longer lengths of stay and higher mortality rates compared to patients with normal renal function. However, the lengths of stay and the mortality rates reported here are unadjusted and warrant further examination.

Discussion

Our study demonstrated that 18% of patients undergoing cardiac bypass surgical procedures developed or had pre-existing renal dysfunction. These patients incurred significantly higher direct hospital costs compared to patients with normal renal function after adjusting for patient age, sex, comorbidities, and race. Longer lengths of stay, higher use of ICU services, more laboratory and radiology testing, and higher pharmacy costs likely drive the higher costs.

These data are consistent with prior studies evaluating the economic impact of major complications after bypass surgery. In a single-institution study, Naglie and colleagues [30] reported \$15,600 in direct hospital costs for elective, uncomplicated bypass patients. In contrast, elective patients with significant postsurgical complications averaged \$23,700 in direct hospital costs. Although in this study major postsurgical complications were broadly defined, these data are of the same relative magnitude as are the data reported here. Similarly, Mangano et al. [22] report increased hospital-based resource utilization among patients with renal dysfunction after cardiopulmonary bypass surgery. In that study, patients with renal failure had more days in the ICU (6.5 vs. 3.1 days) and significantly longer hospital stay (18.2 vs. 10.6 days). Additionally, renal patients were three times as likely to be discharged to a long-term care facility.

There are several limitations that must be considered when interpreting this study. We include only hospital direct costs in this study. Professional fees billed by physicians are not included, nor are hospital indirect costs (which are difficult to interpret). Additionally, this is a single-institution study, and the costs reported are relevant to this particular institution. However, the magnitude of the increased costs is consistent with prior studies and may be generalizable to other institutions. The rate

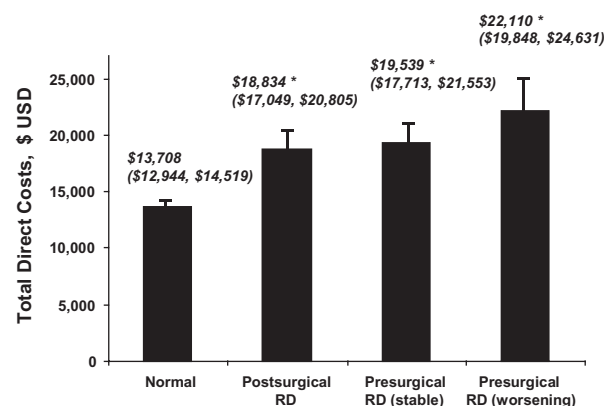


Figure 2 Hospital cost associated with renal dysfunction after cardiopulmonary bypass surgery. Least-squares means and their respective 95% CIs are presented for each study subgroup: 1) normal renal function; 2) postsurgical renal dysfunction; 3) presurgical renal dysfunction (stable); and 4) presurgical renal dysfunction (worsening). Definitions for the four subgroups can be found in the text. All cost data are presented as back-transformed (exponentiated) values (i.e., geometric means). We also report pairwise comparisons of the adjusted means for log TDHC to the normal renal function subgroup. *For each preplanned group comparison with the normal group (on the log scale), all P values are < .0001. RD, renal dysfunction.

of renal failure also may be different at other institutions; the study site is a large academic medical center and receives many complicated referrals as well as re-operations, which may increase the risk of renal failure. Finally, owing to inherent limitations in our administrative data set, we were unable to identify hemodialysis status among our presurgical subgroups. Thus, these presurgical subgroups (presurgical subgroups [stable] and presurgical [worsening]) contain a mixture of patients with chronic renal insufficiency and chronic renal failure requiring hemodialysis.

In our study, cardiopulmonary bypass patients with renal dysfunction averaged \$5807 higher costs per admission compared to patients with normal renal function. This cost difference translates to \$3.7 million in additional costs incurred by the study institution over the 3-year study period, approximately half of which is attributable to new-onset postsurgical renal dysfunction. This latter postsurgical subgroup, the 9% of patients admitted with normal renal function who developed renal dysfunction during their hospitalization, is an important subgroup because it is in this postsurgical subgroup that prevention of the renal dysfunction may significantly reduce direct hospital costs. Additionally, our data confirm that patients with pre-existing but stable renal dysfunction demonstrate significantly greater total direct hospital costs than do normal controls and that patients with pre-existing but worsening renal dysfunction are more costly still. From an economic perspective, these data highlight the importance of clinical strategies that optimize renal function in all patients that undergo cardiopulmonary bypass surgery. Such interventions could potentially include: 1) improved preoperative screening to identify high-risk patients; 2) improved monitoring of intraoperative and postoperative volume status; 3) careful avoidance of nephrotoxic agents; and finally 4) pharmacologic interventions that improve glomerular filtration and renal blood flow, thereby providing a physiologic environment of heightened renovascular protection.

Conclusion

From the data presented, we conclude that interventions that reduce the incidence of renal dysfunction, or that ameliorate the worsening of pre-existing renal dysfunction, may be significantly cost saving. Nationwide there are 607,000 cardiac bypass graft surgeries done on an annual basis. Using data from this investigation, we estimate that

the increased hospital direct costs associated with renal dysfunction for cardiopulmonary bypass patients across the United States is approximately \$643 million. These incremental costs are primarily borne by hospitals, who under most reimbursement methodologies are unable to bill patients or payers for these additional expenditures. Thus interventions or pharmacotherapies that can reduce the incidence of renal dysfunction in patients undergoing cardiopulmonary bypass procedures are likely to be cost-effective.

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References

- 1 American Heart Association. 2001 Heart and Stroke Statistical Update. Dallas (TX): The Association, 2000.
- 2 Ugnat AM, Naylor CD. Trends in coronary artery bypass grafting in Ontario from 1981 to 1989. *CMAJ* 1993;148:569-75.
- 3 Platt GH, Svenson LW, Woodhead SE. Coronary artery bypass grafting in Alberta from 1984 to 1989. *Can J Cardiol* 1993;9:621-4.
- 4 Naylor CD, Ugnat AM, Weinkauff D, et al. Coronary artery bypass grafting in Canada: what is its rate of use? Which rate is right? *CMAJ* 1992; 146:851-9.
- 5 Haraphongse M, Na-Ayudhya RK, Teo KK, et al. The changing clinical profile of coronary artery bypass graft patients, 1970-89. *Can J Cardiol* 1994;10:71-6.
- 6 Anderson GM, Grumbach K, Luft HS, et al. Use of coronary artery bypass surgery in the United States and Canada: influence of age and income. *JAMA* 1993;269:1661-6.
- 7 Christakis GT, Ivanov J, Weisel RD, et al. The changing pattern of coronary artery bypass surgery. *Circulation* 1989;80:1151-61.
- 8 Peterson ED, Jollis JG, Bebbchuk JD, et al. Changes in mortality after myocardial revascularization in the elderly: the national Medicare experience. *Ann Intern Med* 1994;121:919-27.
- 9 Peterson ED, Cowper PA, Jollis JG, et al. Outcomes of coronary artery bypass graft surgery in 24,461 patients aged 80 years or older. *Circulation* 1995;92:II85-91.
- 10 Abramov D, Tamariz MG, Fremes SE, et al. Trends

- in coronary artery bypass surgery results: a recent, 9-year study. *Ann Thorac Surg* 2000;70:84–90.
- 11 Shaw PJ, Bates D, Cartlidge NE, et al. Neurologic and neuropsychological morbidity following major surgery: comparison of coronary artery bypass and peripheral vascular surgery. *Stroke* 1987;18:700–7.
 - 12 Jones EL, Weintraub WS, Craver JM, et al. Coronary bypass surgery: is the operation different today? *J Thorac Cardiovasc Surg* 1991;101:108–15.
 - 13 Mangano DT. Perioperative cardiac morbidity. *Anesthesiology* 1990;72:153–84.
 - 14 Hammermeister KE, Burchiel C, Johnson R, Grover FL. Identification of patients at greatest risk for developing major complications at cardiac surgery. *Circulation* 1990;82:IV380–9.
 - 15 Reves JG, Karp RB, Buttner EE, et al. Neuronal and adrenomedullary catecholamine release in response to cardiopulmonary bypass in man. *Circulation* 1982;66:49–55.
 - 16 Mazzarella V, Gallucci MT, Tozzo C, et al. Renal function in patients undergoing cardiopulmonary bypass operations. *J Thorac Cardiovasc Surg* 1992;104:1625–7.
 - 17 Mori A, Watanabe K, Onoe M, et al. Regional blood flow in the liver, pancreas and kidney during pulsatile and nonpulsatile perfusion under profound hypothermia. *Jpn Circ J* 1988;52:219–27.
 - 18 Yeboah ED, Petrie A, Peard JL. Acute renal failure and open heart surgery. *BMJ* 1972;1:415–8.
 - 19 Abel RM, Wick J, Beck CH Jr, et al. Renal dysfunction following open-heart operations. *Arch Surg* 1974;108:175–7.
 - 20 Abel RM, Buckley MJ, Austen WG, et al. Etiology, incidence, and prognosis of renal failure following cardiac operations: results of a prospective analysis of 500 consecutive patients. *J Thorac Cardiovasc Surg* 1976;71:323–33.
 - 21 Bhat JG, Gluck MC, Lowenstein J, Baldwin DS. Renal failure after open heart surgery. *Ann Intern Med* 1976;84:677–82.
 - 22 Mangano CM, Diamondstone LS, Ramsay JG, et al. Renal dysfunction after myocardial revascularization: risk factors, adverse outcomes, and hospital resource utilization. The Multicenter Study of Perioperative Ischemia Research Group. *Ann Intern Med* 1998;128:194–203.
 - 23 Stott RB, Cameron JS, Ogg CS, Bewick M. High mortality in acute renal failure. *Lancet* 1972;2:598.
 - 24 Montgomerie JZ, Kalmanson GM, Guze LB. Renal failure and infection. *Medicine (Baltimore)* 1968;47:1–32.
 - 25 Robicsek F. Effect of risk factors on the costs of coronary surgery. *Am J Cardiol* 2000;85:1338–9.
 - 26 Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373–83.
 - 27 Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol* 1992;45:613–9.
 - 28 Hlatky MA, Rogers WJ, Johnstone I, et al. Medical care costs and quality of life after randomization to coronary angioplasty or coronary bypass surgery. Bypass Angioplasty Revascularization Investigation (BARI) Investigators. *N Engl J Med* 1997;336:92–9.
 - 29 Weintraub WS, Craver JM, Jones EL, et al. Improving cost and outcome of coronary surgery. *Circulation* 1998;98:II23–8.
 - 30 Naglie G, Tansey C, Krahn MD, et al. Direct costs of coronary artery bypass grafting in patients aged 65 years or more and those under age 65. *CMAJ* 1999;160:805–11.